In the Specification

Please amend the description of Figures 3, 4, 5 and 6 on pages 6 and 7 as follows:

Figure 3: Multisequence nucleic acid alignment of cDNAs encoding human Futrin 1 (SEQ ID NO: 20),2 (SEQ ID NO: 21, 3 (SEQ ID NO: 22) and 4 (SEQ ID NO: 23) and Xenopus Futrin 1 (SEQ ID NO: 24) Identical nucleotides are highlighted in black. All nucleic acid sequences begin with the translation initiator ATG codon indicated with an asterisk.

Figure 4: Multisequence amino acid alignment of human Futrin 1 (SEQ ID NO: 25),2 (SEQ ID NO: 26) 3 (SEQ ID NO: 27) and 4 (SEQ ID NO: 28) deduced from human cDNAs (see Figure 3) Identical amino acids are highlighted in black, similar amino acids are in grey.

Figure 5 A and B: Futrins promote Wnt signalling Cotransfection experiments in 293T cells. Wnt-responsive luciferase reporter assays were performed in 96 well plates in triplicates as described (Wu et al., Curr Biol 10 (2000), 1611-1614). Luciferase activity was normalized against Renilla activity using a commercial kit (Clonetech). Wntl = mouse Wntl, fz8 = mouse frizzled8, Futrinl = xenopus Futrin 1, Wnt3A = mouse Wnt3A, (0. lng) in A indicates amount of plasmid DNA transfected per well, RLU: relative luciferase units

Figure 6: Sequence comparison of human Rspo proteins (hR-spondin 1 (SEQ ID NO: 29), hR-spondin 2 (SEQ ID NO: 30), hR-spondin 3 (SEQ ID NO: 31), hR-spondin 4 (SEQ ID NO: 32) ~~to 4~~) (A) Alignment of human (h) Rspo proteins (corresponding to the alignments of human Futl-4 in Figure 4 except that different

designations are used). The signal peptide, furin- like domains and thrombospondin type 1 domain are underlined and conserved amino acids are shown in black. (B, C) Rspo homology matrix showing overview of amino acid identity in % between human Rspo proteins (B) and between Xenopus (X) or mouse (m) Rspo2 and human Rspo proteins, respectively (C).

Please amend the description of Figure 15 on the bottom of page 12 and top of page 13 as follows:

Figure 15: Futrin expression is deregulated in various human tumors. The expression of Futrin 1 (A), 2 (B), 3 (C) and-4 (D) or ubiquitin (E) (to show equal loading) was analysed by radioactive hybridisation on arrayed mRNAs (Clontech, Cancer Profiling Array II) from normal and cancerous tissue samples from different patients. Abbreviations N, normal tissues; T, tumor tissues.

Please amend the first paragraph on top of page 37 as follows;

(D) Morpholino antisense oligonucleotides and siRNA constructs The 5'nucleotide sequence of an additional (pseudo-) allele for Xenopus Rspo2 gene was obtained using 5'RACE (GeneRacer kit, Invitrogen). Based on these sequences, an antisense morpholino oligonucleotide targeting both pseudoalleles around the ATG start codon was designed (Rspo2Mo): GCCGTCCAAATGCAGTTTCAAC (SEQ ID NO: 1). pSuper constructs producing siRNA against human Rspo 2,3 or a non-sense control were made according to Brummelkamp et al., Science 296 (2002), 550-3. The sequences are: human Rspo2, TCCCATTTGCAAGGGTTGT (SEQ ID NO: 2); human Rspo3, AGCTGACTGTGATACCTGT (SEQ ID NO: 3); non- sense control, ACTACCGTTGTTATAGGTG (SEQ ID NO: 4).

Please amend the top of page 38 as follows:

(forward, GAATGCCCAGAAGGATTTGC (SEQ ID NO: 5); reverse, GGGATGGTGTCTTTTGCTGG (SEQ ID NO: 6)); Xenopus Rspo3 (forward, GAAGCAAATTGGAGTCTGTCG (SEQ ID NO: 7); reverse, GATTGTTCTCAAACCCTTCAGG (SEQ ID NO: 8)); human Rspo1 (forward, ACAGACACAAGACACACACGC (SEQ ID NO: 9); reverse, TGTCTTCTGGTGGCCTCAG (SEQ ID NO: 10)) human Rspo2 (forward, CCGAGCCCCAGATATGAAC (SEQ ID NO: 11); reverse, TGACCAACTTCACATCCTTCC (SEQ ID NO: 12)); human Rspo3 (forward, AGGGACTGAAACACGGGTC (SEQ ID NO: 13); reverse, TGTCTTCTGGTGGCCTCAG (SEQ ID NO: 14)); human Rspo4 (forward, AAGCTGGGACACAGCACAG (SEQ ID NO: 15); reverse, GAAGCCTTGGAGCCTTGTC (SEQ ID NO: 16)).

Please amend the first paragraph on page 41 as follows:

Futrins are required for full Wnt signalling To test the requirement of Futrins in Wnt signalling, siRNA mediated gene knock-out was utilized (Brummelkamp et al., Science. 2002,296 (5567): 550-3). Hela cells were transfected using Lipofectamine Plus with 80ng Wnt reporter 7LEF-Rev- fosLuc, 10 ng pRL-TK (Promega) and 300 ng pSuper constructs (Brummelkamp et al.) that produce either siRNA against human Futrinl and 2, or a nonsense control. 7LEF-Rev-fosLuc reporter construct containing seven LEF binding sites in front of minimal fos promoter followed by firefly luciferase ORF was kindly provided by R. Grosschedl (Howard Hughes Medical Institute). pSuper constructs contain 19-nucleotide sequences from human Futrinl (sequence: TCCCATTTGCAAGGGTTGT (SEQ ID NO: 17)), human Futrin2 (sequence: AGCTGACTGTGATACCTGT (SEQ ID NO: 18)) or control nonsense sequence (ACTACCGTTGTTATAGGTG (SEQ ID NO: 19)).